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Filed : April 2, 2001

### REMARKS

Claims 32-36, 39-50, 59 and 62-68 are pending and stand rejected on a variety of grounds, each of which is addressed below. Claims 32, 59 and 62 are amended herein. The amendments are fully supported by the specification as filed. Support for the amendment to Claim 59 can be found in Example 15. The amendment to Claim 62 incorporates the subject matter of Claim 59, from which it previously depended. Support for the amendment to Claim 32 is discussed below.

Applicants would like to thank the Examiner for the opportunity to discuss the present application in a telephone interview on July 23, 2003. The present amendments and comments are consistent with that discussion.

#### Support for Present Amendment to Claim 32 and the Specification

Claim 32 has been amended to recite "deactivating said protease under conditions which produce a water soluble hydrolysate." The specification has been amended to be consistent with the wording of Claim 32. Support for the production of a water soluble hydrolysate in the claimed process can be found, for example, in Example 4. While the solubility in water is not explicitly recited, hydrolysates produced by the claimed method are indicated to have solubilities ranging from 65% to 80%. The solubilities of the hydrolystes are given "across the pH range" and at particular pH. pH is a measure of the concentration of hydrogen ions in water. Thus, a person of skill in the art will recognize that the solvent used to measure the solubility of the hydrolysates was water.

#### Objections to the Specification

The Examiner objected to the previous amendment to the specification and claims under 35 U.S.C. §132 because of the recitation of "conditions which produce a hydrolysate with a solubility of at least 65%." The Examiner found that while a limitation of 65% to 85% would be supported by the specification, the language "at least 65%" encompasses solubilities that are not disclosed. As discussed in the telephone interview on July 23, 2003, Applicants have reconsidered the amendment in view of the Examiner's comments and have concluded that it was not necessary to limit the solubility to a particular range. As a result, the objectionable language in the specification and claims is replaced in the current amendment with the recitation of

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"conditions which produce a water soluble hydrolysate." Thus, Applicants submit that the Examiner's objections should be withdrawn.

Claim Rejections Under 35 U.S.C. §112, first paragraph

Claims 32-36, 39-50, 59 and 62-66 were rejected under 35 U.S.C. §112, first paragraph, for the recitation of "bio-activity." The Examiner found that this language encompassed many different biological activities that were not supported by the disclosure. Without acquiescing in the Examiner's position, Applicants have amended Claim 32 to recite a biological activity selected from the group consisting of angiotensin converting enzyme inhibiting activity and *in vivo* blood pressure reduction. These activities are supported in the specification at Examples 13 and 16, respectively.

In addition the Examiner based this rejection on the recitation of "at least 65%" in Claim 32. As discussed above, the objectionable language has been replaced with language that is fully supported by the specification as filed.

In view of the present amendments, Applicants submit that the rejections under 35 U.S.C. §112, first paragraph, should be withdrawn.

Claim Rejections Under 35 U.S.C. §112, second paragraph

Claims 32-36, 39-50, 59 and 62-68 were rejected under 35 U.S.C. §112, second paragraph based on the recitation of solubility in Claim 32 without an indication of the solvent to be used to determine solubility.

Claim 32 has been amended to indicate that the solubility is measured in water. In view of this amendment, the rejection under §112, second paragraph, should be withdrawn.

Claim Rejections Under 35 U.S.C. §102

The Examiner rejected Claims 32, 39, 45, 50 and 63 under 35 U.S.C. §102(b) as anticipated by Mellqvist et al. (U.S. Patent No. 4,847,096).

Mellqvist et al. fails to teach or suggest testing a hydrolysate for a bioactivity selected from the group consisting of ACE inhibiting activity and reduction of *in vivo* blood pressure, as required by amended Claim 32. Claims 39, 45, 50 and 63 depend from Claim 32. Thus, Applicants request withdrawal of this rejection.

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Claim Rejections Under 35 U.S.C. §103

Claims 32-36, 39, 40, 42-44 and 46-49 were rejected under 35 U.S.C. §103(a) as unpatentable over Mellqvist et al. As discussed above, Mellqvist fails to teach or suggest testing a hydrolysate for a biological activity selected from the group consisting of angiotensin converting enzyme inhibiting activity and reduction of *in vivo* blood pressure, as recited in Claim 32. The remaining claims depend from Claim 32. Thus, Applicants request withdrawal of this rejection.

Claims 32 and 41 were rejected over the combination of Mellqvist and Shimamura et al. (EP 0799577). As Shimamura does not teach or suggest testing a hydrolysate for a biological activity, this rejection should be withdrawn.

Claims 32, 45 and 49 were rejected over the combination of Mellqvist and Soehnlen (U.S. Patent No. 4,358,464). Soehnlen does not make up for the deficiencies of Mellqvist. Thus, this rejection should be withdrawn as well.

The Office Action also states that Claims 32 and 62-68 were rejected over the combination of Mellqvist and Mullally (Int. Dairy Journal 7:299-303 (1997)). However, the Examiner goes on to state that Claim 32 stands rejected as obvious over Melqvist alone and only applies the combination of references to dependent Claims 62-68. As discussed above, Melqvist does not teach or suggest the claimed process. However, Claim 32 has been amended herein to refer to testing the hydrolysate for a bioactivity selected from the group consisting of ACE inhibiting activity and reduction of *in vivo* blood pressure. As the testing for ACE inhibiting activity is mentioned in Claims 67 and 68, which were rejected over the combination of references, the substance of the rejection is discussed below.

The Examiner found that Mellqvist differs from the claims in not disclosing the use of the enzymatic hydrolysate in assays of angiotensin converting enzyme inhibition. Further, he found that Mullally "clearly discloses that hydrolysates of whey produced by proteases having a variety of specificities all possess anti-hypertensive activity." The Examiner concluded that in view of Mullally, the artisan of ordinary skill would have been motivated to test the digests of Melqvist for anti-hypertensive properties, particularly ACE inhibiting activity.

Applicants respectfully disagree with the Examiner and submit that there is no motivation to combine the references. First, Mellqvist is concerned with separating the fat from whey

protein concentrates. There is no teaching or suggestion in Mellqvist that the hydrolysates they produced have or are likely to have antihypertensive properties. Thus, there is no teaching or suggestion in Mellqvist to test the hydrolysates for ACE inhibiting activity as described in Mullally.

Conversely, Mullally does not use the process disclosed by Mellqvist or suggest that the process used by Mellqvist would produce a hydrolysate with antihypertensive activities. While Mullally tests several enzymes for their ability to produce whey protein hydrolysates with ACE inhibiting activity, she does not use the enzyme used by Mellqvist and does not teach or suggest that all enzymes or all process will produce whey protein hydrolysates with antihypertensive activities. One of skill in the art would recognize that the nature of the enzyme used for the proteolysis will determine the activity of the peptides in the hydrolysate.

Further, Mullally only teaches processes in which protease activity is stopped by heating to high temperature for an extended period of time. One of skill in the art will recognize that such treatment changes the conformation of the proteins and peptides in the hydrolysate, and produces a hydrolysate comprising insoluble proteins. Changes in protein conformation would be expected to affect the activity of the hydrolysate.

There is no teaching or suggestion in Mullally that a process that produces a soluble hydrolysate would result in a hydrolysate with the same activity as a process that changes the conformation of the proteins in the hydrolysate. The teachings are even less relevant to a soluble hydrolysate that is produced from a different enzyme with a different specificity, as taught in Mellqvist.

Because there is no teaching or suggestion in Mullally that a process using the enzymes and conditions disclosed in Mellqvist would produce a hydrolysate with ACE inhibiting activity, one of skill in the art would not be motivated by the teachings of Mullally to test hydrolysates produced by Mellqvist for biological activity. Thus, Applicants submit that Claim 32, as amended, is not obvious over Mellqvist in view of Mullally.

#### Claim Rejections Under 35 U.S.C. §102/§103

Claim 59 was rejected as anticipated by or obvious over Mellqvist. In particular, the Examiner found that the hydrolysate produced by Mellqvist would be expected to comprise two or more of the peptides recited in Claim 59. Without acquiescing in the Examiner's position,

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Claim 59 has been amended to recite an isolate peptide. Mellqvist does not teach or suggest isolating any of the recited peptides. Thus, Applicants request withdrawal of this rejection.

Conclusion

For the reasons presented above, Applicants respectfully submit that the present application is in condition for allowance. If any issues remain, the Examiner is invited to contact Applicants' counsel at the number provided below in order to resolve such issues promptly.

Respectfully submitted,

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